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Pollutant particles produce vasoconstriction and enhance MAPK signaling via angiotensin type I receptor

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Abbreviations: angiotensin type 1 receptor (AT_1R), particulate matter (PM), human pulmonary artery endothelial cells (HPAECs), nitric oxide (NO), epidermal growth factor receptor (EGFR), angiotensin converting enzyme (ACE), mitogen-activated protein kinase (MAPK), extracellular signal-regulated kinases ½ (ERK1/2).

ABSTRACT

Exposure to particulate matter (PM) is associated with acute cardiovascular mortality and mobidity, but the mechanisms are not entirely clear. In this study, we hypothesized that PM may activate the angiotensin type 1 receptor (AT_1R), a G protein-coupled receptor that regulates inflammation and vascular function. We investigated the acute effects of St. Louis urban particle (UP, SRM1648) on the constriction of isolated rat pulmonary artery rings and the activation of extracellular signal-regulated kinases1/2 (ERK1/2) and p38 mitogen-activated protein kinases (MAPKs) in human pulmonary artery endothelial cells (HPAECs) with or without losartan, an antagonist of AT_1R. UP at 1-100 μg/ml induced acute vasoconstriction in pulmonary artery. UP also produced a time- and dose-dependent increase in phosphorylation of ERK1/2 and p38 MAPK. Losartan pretreatment inhibited both the vasoconstriction and the activation of ERK1/2 and p38. The water-soluble fraction of UP was sufficient for inducing ERK1/2 and p38 phosphorylation, which was also losartan-inhibitable. Copper and vanadium, two soluble transition metals contained in UP, induced pulmonary vasoconstriction and phosphorylation of ERK1/2 and p38, but only the phosphorylation of p38 was inhibited by losartan. The UP-induced activation of ERK1/2 and p38 was attenuated by captopril, an angiotensin-converting enzyme inhibitor. These results indicate that activation of the local renin-angiotensin system may play an important role in cardiovascular effects induced by PM.